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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/806,645	07/12/2001	Yuri Kolesnikov	830010-2006.	3048

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EXAMINER	
WELLS, LAUREN Q	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 06/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/806,645	KOLESNIKOV ET AL.	
	Examiner	Art Unit	
	Lauren Q Wells	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7-9,14,15 and 19-30* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,7-9,14,15 and 19-30* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/15/04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 7-9, 14-15, 19-30 are pending. The amendment filed 3/15/04, amended claims 1, 9 and 15, cancelled claims 4, 13, 16 and 17, and added claims 19-30.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/15/04 has been entered.

Response to Arguments

Applicant's arguments with respect to claims 1, 7-9, 14-15, 19-30 have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 27-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The instant specification does not provide support for alkylene oxide, ethylene oxide, and hexitol anhydride as excipients in the instant invention. Page 9 of the specification teaches alkylene oxide, ethylene oxide, and

hexitol anhydride as reactants in condensation reactions to produce excipients, but the recitation of alkylene oxide, ethylene oxide, and hexitol anhydride as excipients is not supported.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 9, 14, 15, 19-23, 26-27, and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gevirtz et al. (5,635,204) in view of Nelson et al. (5,840,731) and in view of Needham et al. (6,261,582), and in view of Caruso (5,891,885).

The instant invention is directed toward a composition comprising ketamine and morphine and a pharmaceutically acceptable topical excipient, wherein the excipient is an aqueous excipient or a gel excipient, and a method of providing analgesia to a mammal comprising topically administering an effective dose of ketamine in combination with morphine.

Gevirtz et al. teach a method for transdermal induction of anesthesia, analgesia or sedation by simultaneously, transdermally administering fentanyl, an alpha adrenergic agonist, and ketamine. Disclosed is a method of inducing anesthesia comprising transdermally administering via a transdermal patch to the skin an amnesia producing drug selected from scopolamine, ketamine, and benzodiazepines, and after an amnesic state is produced, transdermally administering amounts of clonidine and fentanyl. Exemplified in the patches are carriers. Thus, the instant invention and Gevirtz et al. both teach a composition comprising an NMDA receptor antagonist (ketamine), an analgesic (fentanyl), and an excipient/carrier

(polyisobutylene), and a method of applying the composition to the skin. See Example 1; Col. 5, line 35-Col. 6, line 50. The reference lacks morphine, preferred excipients and the percent weight of ketamine based on the total weight of ketamine and morphine.

Nelson et al. teach a method and apparatus for administering analgesics. Fentanyl and morphine are disclosed as interchangeable analgesics that act on opiod pain receptors. See Col. 4, lines 11-42.

Needham et al. teach surgical methods and compositions thereof. Fentanyl and morphine are disclosed as interchangeable and combinable analgesics. See Col. 2, lines 60-64; Col. 15, lines 24-26.

Caruso teaches pharmaceutical formulations for treating migraines. The reference teaches creams, gels, ointments, lotions, and transdermal patches as interchangeable formulations for topical administration, see col. 6, lines 26-32. The reference teaches that such compositions can be formulated with an aqueous or oily base with the addition of suitable thickening, gelling, emulsifying, stabilizing, dispersing, suspending, and/or coloring agents, see col. 6, lines 26-32. For sodium carboxymethyl cellulose, methylcellulose, hydroxypropymethylcellulsoe, gum acacia, condensation products of ethylene oxide (wetting agent) and others as excipients, see Col. 7, lines 8-27.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the fentanyl of Gevirtz et al. for morphine because a) Gevirtz et al., Nelson et al, and Needham et al. are all directed to analgesic compositions; b) Nelson et al. and Needham et al. teach morphine and fentanyl as interchangeable opiod pain receptor analgesics; thus, one of ordinary skill in the art would be motivated to substitute morphine for fentanyl in the

compositions of Gevirtz et al. because of the expectation of producing similar analgesic effects via the opiod pain receptor.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to exemplify the transdermal patch of Gevirtz et al. in an aqueous or gel excipient that is applied as an aqueous solution or gel a) because Caruso teaches gels, aqueous solutions, and transdermal patches as interchangeable formulations for topical administration of a pharmaceutical for relieving pain; b) because of the expectation of achieving a product with equivalent pain relief.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to teach ethylene oxide, as taught by Caruso, as an excipient in the compositions of Gevirtz et al., because of the expectation of achieving a formulation, wherein the surface tension of the liquid is reduced, thereby causing the liquid to spread across or penetrate more easily the surface of a solid (function of a wetting agent).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to teach the ketamine of the combined references as comprising 0.1-5% of the total weight of ketamine and morphine because it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. In re Aller, 105 USPQ 233.

Regarding claims 1, 7-8, 19-20, 23-30, it is respectfully pointed that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). In the instant case, the intended use does not result in a structural difference.

The claims are directed to a method of providing peripheral analgesia and not central or system analgesia to a mammal and a method of providing a tolerance attenuating analgesia to a mammal with pre-existing tolerance to an analgesic comprising topically administering a composition comprising a tolerance-attenuating dose of ketamine in combination with morphine. Any properties exhibited by or benefits provided the composition are inherent and are not given patentable weight over the prior art. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties Applicant discloses and/or claims are necessarily present. In re Spada, 911 F.2d 705, 709, 15 USPQ 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01. The burden is shifted to Applicant to show that the prior art product does not inherently possess the same properties as instantly claimed product. The prior art teaches application to the skin of compositions containing the same components as instantly claimed, which would inherently provide peripheral analgesia and not central or system analgesia as instantly claimed. Applicant has not provided any evidence of record to show that the prior art compositions do not exhibit the same properties as instantly claimed.

It is further respectfully pointed out that a compound and its properties are inseparable and since morphine is administered by the above prior art in the same way as that in the instant invention, the morphine of the prior art functions through the peripheral opiate receptor.

Claims 7-8, 24-25, 28-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over

Gevirtz et al. in view of Nelson et al., Needham et al., and Caruso as applied to claims 1, 9, 14, 15, 19-23, 26-27, and 30above, and further in view of Kaneko et al (Anesthesiology '94).

Gevirtz et al., Nelson et al., and Needham et al. are applied as discussed above. The reference lacks a local anesthetic.

Kaneko et al. teach the synergistic antinociceptive interaction after epidural coadministration of morphine and lidocaine. See background.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to add the lidocaine of Kaneko et al. to the composition of the combined references because of the expectation of achieving synergistic analgesia, and hence, enhanced pain relief.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lauren Q Wells whose telephone number is 571-272-0634. The examiner can normally be reached on M&R (5:30-4).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

lqw

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER